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Presurgical cognitive deficits in patients receiving coronary artery bypass graft surgery

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Abstract

Coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass (CPB) can produce a higher incidence of neuropsychological complications than other types of highly invasive noncardiac vascular surgery. Cognitive complications most likely arise from either embolization or hypoxia. An alternative surgical procedure has been developed that allows CABG to be performed without stopping the heart ("off-pump" CABG, or OPCABG). This study examined the neuropsychological performance of patients undergoing OPCABG, hypothesizing that patients undergoing OPCABG would show fewer cognitive deficits than patients whose hearts were stopped. A 1-hr neuropsychological battery was administered preoperatively to 43 patients before prospective randomization to either CPB CABG or OPCABG, and again to 34 of those patients 2 to 3 months postoperatively by an examiner blind to surgical condition. Neuropsychological status did not change 2.5 months postsurgically in either OPCABG or CABG groups. However, both groups showed dramatic presurgical cognitive deficits in multiple domains, particularly verbal memory and psychomotor speed. This corroborates previous research suggesting that patients requiring CABG surgery may evidence significant presurgical cognitive deficits as a result of existing vascular disease. (*JINS*, 2003, *9*, 913–924.)

Keywords: OPCABG, Neuropsychological scores, Coronary artery bypass, Cardiovascular diseases

INTRODUCTION

For the past 50 years, coronary artery bypass graft (CABG) surgery has been the standard method by which one or more major cardiac blood vessels is replaced after being damaged by coronary artery disease. Approximately 800,000 CABG procedures are performed per year worldwide. Neuropsychological deficits have been observed in 33% to 83% of CABG patients postsurgically, persisting after 12 months in up to 35% of these patients (Barbut & Caplan, 1997; Gill & Murkin, 1996; Newman et al., 1996). A recent study found that 42% of patients evidenced cognitive deficits 5 years after CABG (Newman et al., 2001). Brain complications after cardiac surgery are generally believed to arise from either embolization or the hypoxia that results from inadequate perfusion (Blauth, 1995; Harrison, 1995; McLean & Wong, 1996; Newman et al., 1995a; Sotaniemi, 1995).

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It is undisputed that some proportion of patients develop at least temporary cognitive complications after CABG surgery using cardiopulmonary bypass pump (CPB). Studies examining these patients at the time of their discharge have found postoperative declines in verbal and visual learning and memory, complex attention, information processing speed, and psychomotor speed in up to 70% of patients (Blumenthal et al., 1991; Croughwell et al., 1994; Newman et al., 1994, 1995b). When CPB patients are assessed 1 week after surgery, deficits in these same domains are found (Chabot et al., 1997; Engelhardt et al., 1996; Mora et al., 1996; Plourde et al., 1997).

Longitudinal examination of these deficits, however, has yielded conflicting reports. A number of studies suggest that partial, if not complete, resolution of symptoms may occur sometime between 2 and 6 months after surgery, while others suggest deficits persist up to 5 years post-CABG. Some studies finding deficits in verbal memory, attention, and psychomotor speed during the first week after CABG surgery have seen these symptoms resolve after 2 months

(Chabot et al., 1997; McLean et al., 1994; Newman et al., 1987), or after 6 months (Vingerhoets et al., 1996a). Others have found that these deficits resolved in some, but not all, of their patients after 1 month (Mora et al., 1996), or that these deficits were not significantly resolved after 2 months (Heyer et al., 1997), or even after 12 months (Gill & Murkin, 1996; Newman et al., 1996). A recent comprehensive study of 261 CABG patients found cognitive deficits in 53% of patients at discharge, 36% after 6 weeks, 24% after 6 months, and 42% after 5 years (Newman et al., 2001).

During the past few years, a new surgical technique has been introduced in which CABG is done without arresting the heart or rerouting circulation through the cardiopulmonary bypass machine. Instead, surgeons chemically slow the heart to 40 beats per minute and mechanically stabilize it so that the graft can be done despite the continuous beating of the heart. There are a number of variations on this procedure, some of which are done via a thoracotomy rather than by opening the sternum. Preliminary reports of "off-pump" CABG (OPCABG) suggest that many of the complications that normally occur as a result of CABG with CPB are reduced or eliminated (Arom et al., 1997; Borst et al., 1996; Calafiore et al., 1997; Gill et al., 1997; Grundeman et al., 1997; Jansen et al., 1997; Subramanian, 1997; Van Dijk et al., 2001). These include reducing incidence of postoperative stroke, myocardial dysfunction or infarction, renal dysfunction, and the multiorgan inflammatory response that occurs in CPB patients (Harris et al., 1993). There is decreased incidence of lung edema, and the improvement in lung functioning may result in lower postsurgical intubation time. The rate of postoperative bleeding may also be decreased, so blood transfusions may be reduced or avoided altogether.

This study examined the cognitive functioning in CABG patients who were prospectively randomized to traditional CABG surgery or OPCABG. This study was designed to determine whether the same neuropsychological deficits that have been demonstrated after traditional on-pump CABG surgery occur when the heart–lung bypass machine is not used. We hypothesized that the OPCABG patients would experience a lower incidence of neuropsychological complications from pretesting to posttesting than the on-pump group, particularly in the areas of verbal and nonverbal memory, psychomotor and information processing speed, and executive functioning. Because all of the patients in this study had some degree of cardiovascular disease, we also hypothesized that the preoperative test scores for both groups would show some deficits in memory, speed, and executive functioning.

METHOD

Research Participants

Forty-three patients were selected to participate in the study because they were scheduled to undergo CABG of either the left anterior descending artery and/or the right coronary artery at Kaiser Sunset Hospital in Los Angeles with the same surgical team. All participants consented in writing to be randomized to CABG or OBCABG, and gave separate written informed consent to undergo neuropsychological assessment. At the time of their presurgical neuropsychological testing, a brief interview was administered to collect information on the patient's date of birth, ethnicity, marital status, education level, medical history (including history of stroke, seizures, general anesthesia, and other brain-related events as well as general systemic medical problems such as hypertension or diabetes), substance use history, history of head trauma or loss of consciousness, and current medications. The Symptom Checklist-90 (Derogatis, 1975) was administered to assess psychological status. Patients were not excluded on the basis of any of these variables, but this information was used to determine if the randomization was effective with respect to prior medical history.

Determination of anatomical eligibility for OPCABG was done by the surgeons after the patient had undergone sternotomy and their vasculature could be visualized. Patient exclusion criteria included (1) target vessels which had anatomy which contraindicated off-pump CABG, including heavily calcified left anterior descending coronary artery (LAD), intramyocardial LAD, and small LAD less than 1 mm in diameter; (2) emergency surgery; (3) hemodynamic instability; (4) target arteries not accessible with cardiac stabilization, that is, circumflex artery; and (5) redo coronary artery bypass surgery. Also, if more than three vessels were determined to require bypass, the patient was considered ineligible for the study.

Four of the 43 patients were excluded because the surgeons examined the cardiac vasculature during surgery and decided that CPB pump would be required to ensure a successful surgical outcome. These four were thus never assigned to a group, as they could no longer be considered to have been randomly assigned to a surgical condition. One patient was randomized to the off-pump condition but was unable to tolerate this procedure and was switched to CPB pump 15 min into the surgery. This was considered a randomization failure and this patient was not included in the collection of cognitive data at Time 2. One patient died 2 weeks postdischarge. Two patients were lost to follow-up because they were unavailable during the retesting period, and one patient refused to be retested. Thus, of the original 43 patients who underwent presurgical neuropsychological assessment, a total of 34 patients were assessed after surgery.

See Table 1 for a summary of the patients' demographic and treatment characteristics. Seventy-seven percent of the patients were Caucasian, with the remaining 23% comprised of African American, Asian American, Latino, and mixed ethnicities. All patients tested were adequately fluent in English to participate in the interview and understand test instructions, though 36% of the patients reported that English was their second language.

Measures

Neuropsychological tests to assess all major domains of cognitive functioning were used. Each test was chosen on the basis of (1) whether it has been standardized and has normative data available, and (2) whether it could be used for retesting within a period of 3 months without significant practice effects, either because it has a valid alternate form or because research has demonstrated that it is not susceptible to practice effects.

Language

The Boston Naming Test (BNT) was used to assess confrontation naming ability. Alternate forms were created by administering all odd-numbered items for the preoperative assessment, and all even-numbered items after surgery. Both the Ross et al. (1995) and the Tombaugh and Hubley (1997) norms were used. The FAS Test was used to assess verbal fluency, using the Tombaugh et al. (1996) norms (as cited in Spreen & Strauss, 1998).

Visuospatial

The copy portion of the Rey–Osterrieth Complex Figure Drawing task was used preoperatively to assess visuospatial functioning, and the Taylor Complex Figure was used postoperatively. The norms used were from Boone et al. (1993). The first subtest of the Ruff Figural Fluency Test was used to assess visuospatial fluency, with norms from Lee et al. (1997). Also, the Judgment of Line Orientation (JLO) Test (forms H and V) was used to assess visuoperceptual accuracy. The norms from Benton et al. (1994) were used.

Attention

The Digits Forward and Backward Test was used as a measure of attention. No alternate form is necessary for this test.

Information processing speed

Part A of the Trailmaking Test was used to assess information processing and visuomotor speed, and the norms used were from Bornstein (1985). The Words and Colors conditions of the Stroop Test were also used to test information processing and articulomotor speed, normed with data from Demick and Harkins (1997).

Verbal memory

The California Verbal Learning Test and its alternate form (Delis et al., 1991) were used to assess various aspects of verbal memory, and both were scored and normed using the computerized scoring program developed by Delis and colleagues.

Nonverbal memory

The delayed drawing of the Rey–Osterrieth and Taylor Complex Figures was used to assess nonverbal memory at preoperative and postoperative testing times, respectively.

Motor speed

The Grooved Pegboard Test was used to assess fine motor coordination and speed bimanually, using Bornstein's norms (1985).

Executive

The Digits Backward score was subtracted from the Digits Forward score to derive a measure of working memory. The Letter/Number Sequencing task as well as the Trails B component of the Trailmaking Test assessed complex sequencing and divided attention. The Stroop C score was used to measure response inhibition. The FAS and Ruff Figural Fluency scores assessed generation of verbal and nonverbal material.

General cognitive

The Mini-Mental State Examination (MMSE) was used to screen the patients' overall level of function in the areas of memory, mental control, praxis, language repetition, and orientation. The norms used for this test were from the Epidemiologic Catchment Area surveys (as cited in Spreen & Strauss, 1998), as well as Crum et al. (1993).

Standardization of cognitive scores

Initial analyses of group differences were performed using the raw data from the neuropsychological tests. However, to further characterize the patients' neuropsychological performance, each raw cognitive score was also converted to a Z score using normative data which took into consideration the patient's age, gender, and education status whenever possible (see individual test descriptions above for specific norms used). Aggregate Z scores were also calculated for each cognitive domain by averaging the Z scores for the individual tests within that domain.

Procedure

This study was reviewed and approved by the Kaiser Permanente Southern California Institutional Review Board. A double-blind, prospective, randomized design was used to assign patients to OPCABG or CABG. The neuropsychological component reported here was part of a broader study designed to evaluate multiple physical outcomes of the two procedures, and detailed information regarding the surgical methods and medical findings has been summarized elsewhere (Kochamba et al., 2000). Before their CABG procedure, patients' baseline cognitive performance was assessed with the neuropsychological testing battery detailed above (number days before surgery: $M = 2.5$, $SD = 5.4$), which

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Table 1. Postsurgical change in cognitive test performance by group

Tests	Time 1 (Mean ± *SD*)	Time 2 (Mean ± *SD*)	*p* value
MMSE			
On pump	27.8 ± 2.21	28.0 ± 2.10	*ns*
Off pump	27.1 ± 2.40	27.8 ± 2.01	
BNT number correct			
On pump	52.0 ± 7.60	52.2 ± 7.13	*ns*
Off pump	55.8 ± 3.63	55.1 ± 4.50	
FAS			
On pump	28.4 ± 15.80	30.8 ± 14.06	*ns*
Off pump	32.7 ± 12.80	32.3 ± 15.06	
CVLT trials 1–5 total			
On pump	37.4 ± 10.08	35.4 ± 10.80	*ns*
Off pump	38.2 ± 9.40	35.2 ± 8.10	
CVLT short delay free			
On pump	6.9 ± 3.63	6.9 ± 3.70	*ns*
Off pump	7.4 ± 2.35	6.3 ± 2.57	
CVLT long delay free			
On pump	7.9 ± 3.95	7.4 ± 3.54	*ns*
Off pump	7.7 ± 3.48	7.3 ± 3.14	
Complex Figure Copy			
On pump	29.9 ± 6.06	31.8 ± 3.91	.048*
Off pump	30.6 ± 5.33	29.7 ± 5.27	
Complex Figure Delay			
On pump	14.5 ± 7.34	20.4 ± 7.67	.007**
Off pump	15.3 ± 6.11	15.7 ± 5.70	
Complex Figure % Retention			
On pump	44.1 ± 22.50	62.7 ± 21.01	*ns*
Off pump	48.5 ± 14.57	54.0 ± 21.33	
JLO			
On pump	22.7 ± 4.59	24.3 ± 4.86	*ns*
Off pump	22.9 ± 3.73	23.0 ± 5.24	
Ruff # Drawings			
On pump	41.3 ± 14.90	37.9 ± 12.06	*ns*
Off pump	43.7 ± 19.33	47.7 ± 14.24	
Ruff % Perseverations			
On pump	10.5 ± 14.10	4.5 ± 6.56	*ns*
Off pump	8.3 ± 10.67	6.6 ± 9.37	
Digit Span total			
On pump	12.8 ± 3.95	12.9 ± 3.81	*ns*
Off pump	13.4 ± 5.33	14.1 ± 4.42	
Letter Number Sequencing			
On pump	7.6 ± 3.49	8.9 ± 2.81	*ns*
Off pump	8.9 ± 2.81	9.0 ± 2.76	
Trails A			
On pump	45.5 ± 24.84	40.5 ± 20.55	*ns*
Off pump	36.0 ± 14.82	37.2 ± 18.82	
Trails B			
On pump	132.5 ± 77.84	121.8 ± 88.51	*ns*
Off pump	90.0 ± 42.93	87.9 ± 45.57	
Stroop Word			
On pump	50.4 ± 12.94	49.7 ± 9.03	*ns*
Off pump	51.3 ± 10.90	49.5 ± 10.07	
Stroop Color			
On pump	73.5 ± 20.74	77.2 ± 36.60	*ns*
Off pump	73.8 ± 18.62	66.2 ± 14.12	

(*continued*)

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Table 1. (*continued*) Postsurgical change in cognitive test performance by group

Tests	Time 1 (Mean ± *SD*)	Time 2 (Mean ± *SD*)	*p* value
Stroop Color/Word			
On pump	163.9 ± 65.99	167.4 ± 85.52	*ns*
Off pump	172.8 ± 77.22	178.3 ± 131.90	
Grooved Pegboard dominant			
On pump	116.7 ± 80.28	89.6 ± 33.21	*ns*
Off pump	95.4 ± 17.89	89.5 ± 15.89	
Grooved Pegboard nondominant			
On pump	136.4 ± 75.32	125.3 ± 65.20	*ns*
Off pump	115.5 ± 40.14	100.2 ± 17.81	
Age			
On pump	62.0 ± 10.42	—	*ns*
Off pump	60.2 ± 9.15	—	
Education			
On pump	13.0 ± 3.37	—	*ns*
Off pump	13.2 ± 1.58	—	
English as second language			
On pump	40%	—	*ns*
Off pump	30%	—	
Sex (% male)			
On pump	83%	—	*ns*
Off pump	71%	—	

Note. * $p < .05$ ** $p < .01$. *ns*: not stated.

lasted approximately 1 hr. Patients who scheduled their surgery in advance were tested preoperatively in their homes (12%) or in the Kaiser offices (12%), and patients who were admitted before they could be contacted regarding their participation in this study were assessed in the hospital (76%). The patients were randomized to either traditional CABG on CPB or OPCABG at the time of surgery. After the surgeons opened the patient's sternum they evaluated the heart's vasculature. If the patient was determined to remain eligible to participate in the study, the surgeons then opened the randomization envelope telling them which type of surgery to perform. Patients were scheduled for follow-up assessment at 10 weeks postsurgery, though there was some variability in actual appointment time due to patient schedule conflicts. Thus, between 2 and 3 months after surgery, the 1-hr postsurgical neuropsychological battery (including the same tests as Time 1 but with appropriate alternate forms) was administered either in the patient's home or in the Kaiser offices (number of days after surgery: $M = 79.7$, $SD = 12.1$). The examiner and patient remained blind to the patient's surgical group placement until after their second assessment was completed.

RESULTS

Verification of Randomization

To determine whether the randomization was effective, the two groups were compared on a number of potential confounds, including (1) testing location (i.e., home *vs.* hospital); (2) medication status; (3) degree of preoperative anxiety, as measured by the SCL-90; (4) degree of distraction during testing, which was measured by the Digits Forward score; (5) number of days before surgery the testing was conducted; (6) history of head injury (loss of consciousness > 5 min); (7) positive history of substance abuse according to the Diagnostic and Statistical Manual, Fourth Edition (DSM–IV) criteria; (8) history of brain-related illness such as stroke, seizures, or brain infection, including sleep apnea or COPD; (9) history of previous heart attack or cardiac arrest; (10) current hypertension, uncontrolled; (11) age; (12) education; and (13) English as second language (ESL) status. Chi-square analyses revealed no significant group differences on any of these variables, thus the patients were considered to have been effectively randomized to the two groups, and no patient characteristic variables were used as covariates during the following analyses.

A one-way ANOVA was run on all Time 1 cognitive test scores to determine if there were any group differences prior to surgery, and no significant group differences were found.

Hypothesis 1: Change in Cognition over Time (Main Effects)

Patients showed a significant change in cognitive test scores over time, independent of surgical treatment. There was

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significant improvement on the Complex Figure Delay (Time 1: 14.8 ± 6.79, Time 2: 18.5 ± 7.26; $p < .005$) and Percent Retention Tests (Time 1: 45.8 ± 19.71, Time 2: 59.4 ± 21.25; $p < .005$). On the California Verbal Learning Test (CVLT), patients also showed a significant decrease in semantic clustering of information and a decrease of both free and cued recall intrusions from Time 1 to Time 2, reflecting a change in style of processing; however, none of the main memory summary scores showed a significant change. There were trends (significant at $p < .10$) towards an increase in serial clustering on the CVLT, but a decrease over time of the total number of words recalled on the CVLT trials 1–5. As expected, there were no significant main effects of group.

Hypothesis 2: Effect of Surgical Status on Cognition (Interaction)

The main hypothesis of this study was that there would be a difference between CABG and OPCABG postsurgical neuropsychological performance. To analyze this, a split plot factorial (repeated measures MANOVA) was done for each neuropsychological test using time as the within-group factor and surgery type as the between-group factor. The Complex Figure Delay showed a significant interaction effect, with the on-pump group evidencing an improvement over time and the off-pump group showing no improvement. Otherwise, no significant group by time interactions were found. See Table 1 for a summary of these results.

To further characterize the interaction effect seen on the Complex Figure Test, two *post-hoc* analyses were done. First, when group differences were reanalyzed holding the Time 1 score constant, the on-pump group had significantly higher scores for both the copy ($p < .031$) and the delay ($p < .006$) at Time 2. Next, the sample was stratified by their overall cognitive performance at Time 1. In the half of the sample that performed worst overall on cognitive testing (low average or below), those in the on-pump condition improved over time while those in the off-pump condition showed no change. However, in the half of the sample that did best overall on cognitive testing (average or above), both on- and off-pump groups improved from Time 1 to Time 2 and the interaction was nonsignificant.

Hypothesis 3: Preoperative Cognitive Deficits (Standardized Scores)

We predicted that all patients would evidence presurgical cognitive deficits regardless of later surgical grouping. A significant proportion of both groups was made up of patients for whom English was a second language (ESL). Though the ESL participants were randomized equivalently to both surgical groups and thus did not influence the analyses of group differences described above, they were expected to artificially lower the overall group scores for the tests primarily measuring the language domain. ANOVAs were run comparing ESL to non-ESL patients on the two primary language measures (the BNT and the FAS), as well as on the word-list memory task (CVLT). As expected, ESL participants were found to have significantly lower scores on both the BNT and the FAS, but there were no significant differences from non-ESL patients on their CVLT performance. Thus, for the following analyses describing preoperative cognitive deficits, ESL patients' BNT and FAS scores were not included in calculations of overall group scores, though their data were included in all other analyses (including the CVLT).

To describe presurgical cognitive deficits, each raw score from the neuropsychological testing was converted into a Z score using appropriate normative data, as described above. Table 2 describes the average Z score and percentile for each cognitive test at both Time 1 and Time 2, regardless of group, and reports the percentile change over time. With the one exception of the number of drawings for the Ruff Figural Fluency Test, for which the group average fell in the 80th percentile at both Time 1 and Time 2, the group scored below the 50th percentile on every test. The group performed at a low average level on the FAS, Complex Figure Copy, Trails B, Stroop Color/Word, Ruff # of Perseverations (which offsets their high percentile level for number of drawings), Digit Span, and CVLT Short and Long Delay Free Recall scores. The sample's mean Z score fell in the impaired range for both the dominant and nondominant hands of the Grooved Pegboard Test and the CVLT trials 1–5 total score.

Aggregate Z scores were also calculated for each cognitive domain by averaging the Z scores for the individual tests within that domain. Using these aggregate Z scores, the participants' mean scores border on the low average range in the Language (27th percentile), Executive (28th percentile), and Attention domains (23rd percentile) before surgery, and they are in the impaired range for Verbal Memory and Perceptuomotor Speed (5th percentile and 3rd percentile, respectively). Table 3 shows the percentage of patients stratified by their level of cognitive function at their Time 1 assessment.

DISCUSSION

The main findings from this study are as follows: (1) Patients did not show significant declines in cognitive functioning at 2.5 months after surgery, regardless of whether they underwent traditional CABG with CPB or the new OPCABG procedure. There was a trend towards an overall decline in verbal memory from Time 1 to Time 2, but generally other cognitive scores either remained constant or significantly improved. (2) There were no significant postsurgical differences in cognitive performance between patients in the OPCABG condition and patients undergoing traditional CABG. (3) Patients evidenced dramatic presurgical cognitive deficits, particularly in the domains of verbal memory and psychomotor speed.

During the time this study was under editorial review, Van Dijk and colleagues (Van Dijk et al., 2002) published a

Table 2. Mean Z scores and percentiles for individual cognitive domain scores (combined surgical groups)

	Before surgery		After surgery		Percentile change
	Mean ± *SD*	Percentile	Mean ± *SD*	Percentile	
MMSE	−.59 ± 1.39	28%	−.43 ± 1.30	33%	+5%
BNT*	−.30 ± 1.36	38%	−.15 ± 1.26	44%	+6%
FAS*	−.97 ± 1.29	17%	−.78 ± 1.23	22%	+5%
CVLT trials 1–5 total	−1.69 ± 3.04	5%	−1.88 ± 3.6	3%	−2%
CVLT short delay free	−1.13 ± 1.10	13%	−1.29 ± 1.13	10%	−3%
CVLT long delay free	−1.00 ± 1.21	16%	−1.06 ± 1.03	14%	−2%
Complex Figure Copy	−1.20 ± 1.72	12%	−1.08 ± 1.58	14%	+2%
Complex Figure Delay	−.43 ± 1.21	33%	.16 ± 1.20	56%	+23%
Complex Figure % retention	−.30 ± 1.17	38%	.47 ± 1.33	68%	+30%
JLO	−.40 ± 0.82	34%	−.22 ± 1.06	41%	+7%
Ruff # Drawings	1.21 ± 2.16	89%	1.00 ± 1.48	84%	−5%
Ruff # Perseverations	−1.07 ± 2.30	14%	−.43 ± 1.59	33%	+19%
Ruff % Perseverations	−.61 ± 1.83	27%	−.07 ± 1.13	47%	+20%
Digit Span total	−.75 ± 0.92	23%	−.60 ± .87	27%	+4%
Letter Number Sequencing	−.46 ± 1.11	32%	−.16 ± 1.04	44%	+12%
Trails A	−.34 ± 1.29	37%	−.30 ± 1.26	38%	+1%
Trails B	−.83 ± 1.47	20%	−.71 ± 1.43	24%	+4%
Stroop Word	−.29 ± 1.11	39%	−.32 ± 0.89	37%	−2%
Stroop Color	−.37 ± 1.12	36%	−.36 ± 1.34	36%	0%
Stroop Color/Word	−1.29 ± 1.48	10%	−1.16 ± 1.76	12%	+2%
Grooved Pegboard dominant	−1.68 ± 1.69	5%	−1.18 ± 1.55	12%	+7%
Grooved Pegboard nondominant	−1.91 ± 1.66	3%	−1.60 ± 1.50	5%	+2%

*Excluding data from participants for whom English was their second language.

much larger randomized study comparing the cognitive effects of on-pump and off-pump CABG, examining 281 patients presurgically as well as at 3 months and 12 months postsurgically. Similar to our study, Van Dijk et al. did not find statistically significant changes in cognitive functioning from baseline to 3 months postsurgery in either surgical group, though they report nonsignificant improvement in most cognitive domains. Thus, though the finding that neither group evidenced significant cognitive declines 2.5 months after surgery was contrary to our expectations, it was not entirely inconsistent with existing studies (Heyer et al., 1997; McLean et al., 1994; Newman et al., 1987; Vingerhoets et al., 1996a, 1996b). We chose the 2–3 month time window to be consistent with the suggestions of investigators who are attempting to establish appropriate methodology for these types of studies, including the Society of Thoracic Surgeons (Murkin et al., 1995). They indicate that cognitive assessment should occur after these initial postoperative deficits have had 2–3 months to resolve, in order to examine whether there are any cognitive effects that could

Table 3. Percent of patients by level of impairment in cognitive domains at Time 1 (combined surgical groups)*

	Percent of patients tested				
	Impaired ($Z \leq -1.70$)	Low average ($-1.70 < Z < -.66$)	Average ($-.67 < Z < +.67$)	High average ($+.66 < Z < +1.70$)	Very superior ($+1.70 \leq Z$)
Language	16.3	16.3	37.2	9.3	0
Visuospatial	7.0	25.6	55.8	11.6	0
Attention	9.3	53.5	20.9	11.6	0
Information processing speed	4.7	23.3	62.8	9.3	0
Verbal memory	48.8	20.9	20.9	0	0
Visual memory	14.0	18.6	46.5	14.0	4.7
Psychomotor speed	51.2	16.3	23.3	2.3	0
Executive	11.6	34.9	46.5	7.0	0
All cognitive	7.0	58.1	34.9	0	0

*Based on aggregate *Z* scores.

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be considered permanent. Though some studies have found cognitive deficits months after surgery in 24–36% of CABG patients (Gill & Murkin, 1996; Newman et al., 1996, 2001), the literature remains mixed. Some studies have failed to yield the expected cognitive deficits after CABG, even during the first week after surgery (McDaid et al., 1994; Regragui et al., 1996). However, with regards to the longer-term benefits of OPCABG, the Van Dijk study's 12-month assessment showed significantly greater improvement on verbal memory testing in the OPCABG group compared to the traditional CABG group (Van Dijk et al., 2002).

It is possible that there are subtle differences in the surgical methodology employed at different hospitals that are causing these diverse results. Numerous perioperative variables increase the patient's risk of cerebral hypoxia during CABG. Induction of hypothermia during surgery has been used routinely to reduce the brain's need for oxygen and to keep neurotransmitters such as glutamate and catecholamines from building up to toxic levels (Barbut & Caplan, 1997; Siesjo et al., 1995). However, ischemic brain damage may be caused by factors involved in the cooling and re-warming processes (Baris et al., 1995; McLean & Wong, 1996; Mutch et al., 1997; Nathan et al., 1995; Newman et al., 1995b, 1996; Van der Linden, 1995). There is evidence that hypoxia may occur regardless of temperature (Baris et al., 1995; Christakis et al., 1995; Croughwell et al., 1994; Mutch et al., 1997). CABG also carries with it a high risk of introducing emboli into the patient's bloodstream from the surgical field, particularly during the process of aortic cannulation, aortic cross-clamp, or the start of cardiopulmonary bypass pump (Barbut et al., 1994; Blauth, 1995; McLean & Wong, 1996). Patient cognitive status has been highly correlated with the number of emboli delivered to the brain during cardiac surgery (Barbut & Caplan, 1997; Jacobs et al., 1998; Moody et al., 1995; Pugsley et al., 1994; Stump et al., 1993; Undar et al., 1998; see also Braekken et al., 1998), though arterial filters may have a protective effect (Mills, 1995). All of the surgeries for both groups were performed by the same surgical team. Hypothetically, both the on-pump and off-pump patients could have been cared for in such a way that the myriad of potential causes of cerebral damage during the course of cardiac surgery and recovery were minimized.

Another possible explanation for the lack of cognitive decline in either group might be that there was a bias inherent in the selection criteria for this study. Studies of the traditional CABG procedure generally do not require the same strict exclusion criteria that had to be maintained in this study in order to select patients able to tolerate the off-pump procedure. This study goes against a trend in which more high-risk individuals are undergoing CABG surgeries and are included in research studies of the procedure (Newman et al., 1995b). People who have more than three arteries to bypass or who have various other types of coronary abnormalities or dysfunction were not eligible for this study, which in turn may make this group somewhat more healthy than other samples of CABG patients whose cognition has been assessed. Increased age heightens the risk for post-CABG brain dysfunction (Mills, 1995; Newman et al., 1995a; Nussmeier, 1994), though this effect cannot be explained by age-related impairments in cerebral blood flow autoregulation during surgery (Newman et al., 1994). However, with a mean age of 61 (SD = 9.4), our sample does not appear significantly younger than patients in other studies yielding different results.

Another possible explanation for the lack of cognitive decline in either group is that a large proportion (77%) of the Time 1 assessments were done in a hospital setting days before the patients underwent major surgery. Ostensibly, there could have been many emotional and environmental distractions from what might have been an optimal baseline assessment at Time 1. However, the fact that there was no significant change in attention score from Time 1 to Time 2 suggests that at least the capacity for simple attention was undisrupted. Also, though the testing battery was designed to minimize the occurrence of practice effects, the previous testing may have influenced the postsurgery test scores to some degree. However, the Complex Figure Copy and Delay were the only tests to show significant improvement over time, suggesting that practice effects, if present, were usually statistically imperceptible.

Given that no cognitive decline was observed in the CABG control group, it is difficult to effectively evaluate the hypothesis that OPCABG is comparatively protective. After data collection for this study was completed, Diegeler et al. (2000) published the results of their study comparing post-surgical cognitive functioning of CABG *versus* OPCABG patients. Using the Canadian Stroke Scale and the Syndrom Kurz Test for their neuropsychological measures, they found that 7 days after surgery, 90% of CABG patients showed at least one impaired score, whereas none of the OPCABG patients did. It is possible that differential cognitive outcome after off-pump *versus* on-pump CABG may only appear during the first weeks after surgery, or conversely, may only begin to appear after 12 months as is suggested by the Van Dijk study (Van Dijk et al., 2002), and thus was not detected in this study.

Though the visuospatial memory test scores were significantly affected by pump status, interpretation of these effects is complicated by a number of factors. The data do not show a significant decline in visual memory performance in the off-pump group; instead, they show that the half of the off-pump group who had the most cognitive deficits at Time 1 failed to show improvement on this task at Time 2. Both the on-pump group and the less cognitively impaired portion of the off-pump sample improved in such a way that they could not be differentiated statistically. There are a number of possible explanations for the observed improvement. In typical administration of the complex figure tasks, patients are not informed that they will be asked to draw the figure again later from memory, thus they do not make the conscious effort to learn the details while copying it. However, at Time 2, some of the patients remembered from the Time 1 testing session that they would be required to recall the figure, and made a conscious effort to learn the figure while copying it, which would naturally result in a significant practice effect. An additional factor is that the Rey–Osterrieth figure was always presented at the Time 1 testing, and the Taylor Figure was always presented at Time 2. However, there has been some suggestion that despite its designation as a valid alternate form, the Taylor Figure may actually be easier than the Rey–Osterrieth figure (Hamby et al., 1993; Tombaugh et al., 1992; Vingerhoets et al., 1998). Thirdly, *post-hoc* analyses suggest that when the variance of Time 1 testing is removed, the on-pump group's copy of the complex figure was significantly better than that of the off-pump group, which might have boosted the on-pump group's ability to remember the drawing. Lastly, it must be considered that, given the number of neuropsychological tests administered in this battery, it is not unexpected that the inflation of Type 1 error would cause at least one test to yield an artificially significant *p* value that would not be replicable in later studies. This issue cannot be resolved by examination of the Van Dijk study's results, as they did not include a comparable measure of visuospatial memory (Van Dijk et al., 2002).

Perhaps the most consequential finding from this study was that the patients in this sample were in the low average to impaired range in nearly every cognitive domain presurgically. Preexisting vascular disease such as enlarged heart, history of previous heart attacks, hypertension, or a longer history of cardiac disease may increase the presurgical incidence of cerebral infarction, embolism, or reduced cerebral blood flow, which may in turn be reflected in greater cognitive deficits (Baird et al., 1997; Boone, 2000; Mills, 1995; Vingerhoets, 1997). The particular cognitive domains found to be most deficient in our sample presurgically (verbal memory and perceptuo-motor speed, where the sample means were in the impaired range) have been repeatedly connected with the types of cerebral events that occur in the course of vascular disease or trauma (Croughwell et al., 1994; Newman et al., 1994; Plourde et al., 1997; Vingerhoets, 1997; Wilson, 1996), and may result from the preexisting vascular problems that have caused these patients to need CABG surgery in the first place. Though the Van Dijk study did not elaborate on presurgical cognitive deficits in their patients, they did report that their patients' verbal-memory and working-memory scores were predominantly in the borderline to impaired range, and their visuospatial and information processing speed scores were in the low average range (Van Dijk et al., 2002).

However, the relationship between these Time 1 impairments and degree of neuropsychological change after CABG is still unclear. It is unlikely that our sample was substantially more cognitively impaired presurgically than patients in studies that found postsurgical declines; however, many studies have neglected to objectively characterize premorbid impairment using normative data or a normal control group, so this comparison cannot be made. The instruments chosen in this study were not susceptible to floor effects, meaning that despite their low Time 1 scores, patients could still have obtained much worse raw scores at Time 2, but did not. However, if it is assumed that cognitive function falls along a normal curve and is susceptible to the phenomenon of "regression to the mean," decreased variance can be expected at either end of the spectrum. Thus, this sample's low scores at Time 1 may have made it less likely that they would show change for the worse as a result of CABG, whereas a cognitively average sample might evidence greater post-CABG decreases in score because of greater available variance.

The results of this preliminary study must be interpreted keeping in mind that power was limited due to the small sample size, and the follow-up interval for testing was relatively short. The generalizability of these findings is necessarily restricted given these factors. However, because CABG surgery is performed on more than half a million patients per year, any major alteration of surgical technique that has the potential to place patients at lower medical risk is worth thorough investigation. While we did not find any indication that OPCABG conveys increased cognitive protection, we also did not find it to be detrimental. Complete neuropsychological assessment of patients' cognitive status during the first postoperative weeks, as well as long-term group comparisons after 6 months and up to 5 years, will be necessary to optimally characterize the nature of cognitive effects of the OPCABG procedure. Also, in order to investigate the possibility that premorbid cognitive deficits are partly mediating postsurgical effects, future studies of CABG must include thorough characterizations of patients' presurgical deficits as well as an analysis of the impact of Time 1 cognitive status on degree of postsurgical change.

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